



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D. C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 6, 2005

MEMORANDUM

SUBJECT: **THIRAM:** Addendum to the HED Human Health Assessment. DP Barcode: D303131 (Chemical ID No. 079801, Case No. 0644)

FROM: Felecia Fort, Chemist/Risk Assessor
Reregistration Branch 1
Health Effects Division (7509C) *FFort*

THRU: Whang Phang, Ph.D, Branch Senior Scientist
Reregistration Branch 1
Health Effects Division (7509C) *WPhang*

TO: Craig Doty, Chemical Review Manager
Special Review and Reregistration Division
Health Effects Division (7508C)

This is an addendum to the HED Human Health Assessment for the Reregistration Eligibility Decision (RED), DP Barcode D293295, dated 12/16/2003 by Felecia Fort. An addendum is required as a result of submissions by the registrant, Taminco N.V., of a developmental neurotoxicity study and a strawberry consumer practices study.

Based on the review of these studies, the following assessments were revised: acute and chronic dietary; residential postapplication, and the occupational handler and postapplication.

EXECUTIVE SUMMARY

The following changes were made to the thiram human health risk assessment.

- **Dietary Endpoint (all durations):** Additional 10X database uncertainty factor is not retained. Previously, the 10X uncertainty factor was applied for lack of DNT study.
- **Acute Dietary- Females 13-49 years old:** The aRfD for females 13+ is 0.014 mg/kg/day based on a NOAEL of 1.4 mg/kg/day from the DNT study. The NOAEL of 1.4

mg/kg/day is based on increases in motor activity seen in female offspring on postnatal day (PND)17 at the LOAEL of 3.7 mg/kg/day.

- **Strawberry processing factor:** A processing factor of 0.42 was applied to strawberries in the dietary assessment.
- **Dermal and Inhalation Endpoints (all Durations):** Source - rat DNT study; NOAEL of 1.4 mg/kg/day; UF = 100 for all populations - additional 10x is not retained (DNT used instead of old endpoints from rat dermal toxicity study and various studies for inhalation).
- **Body Weight:** 60 kg used instead of 70 kg because DNT results apply to females 13+ years old.
- **Exposure Scenarios:** All toddler turf exposures were deleted from the assessment as uses leading to this type of exposure were cancelled by registrant. Additionally, the turf reentry worker transfer coefficients have been modified to reflect latest data (see attached spreadsheet for details). Golf course use was also restricted to greens and tees so the exposure duration for this scenario was reduced from 4 hours to 1 hour.
- **Drinking Water:** EECs used for the aggregate assessment were based on a golf course scenario instead of a turf farm scenario to reflect cancellation by the registrant of the turf farm use.

Dietary Assessment

Based on the above changes, a revised Tier 3 analysis was conducted using field trial residues, processing factors, and percent crop treated (%CT) values provided by the Biological and Economic Analysis Division (BEAD).

The acute and chronic dietary analyses for thiram show that...

- For all registered commodities (strawberry, apple, peach), the acute risk estimates are below the Agency's level of concern at the 99.9th exposure percentile for all population subgroups. The acute dietary exposure estimate for children 1-2 years old, the highest exposed population subgroup, is 78% of the aPAD.
- For all commodities, the chronic risk estimates are below the Agency's level of concern for the general U.S. population (<1% of the cPAD) and all population subgroups. The chronic dietary exposure estimate for children 1-2 years old, the highest exposed population subgroup, is <1% of the cPAD.
- These analyses are based solely on field trial data and could be further refined if monitoring data were available.

Occupational and Residential Exposure Assessment

The overall results indicate that the Agency has risk concerns for some of the marketplaces where thiram is used. Occupational handler risks are generally not of concern at the current label requirements. For those where additional clothing or equipment is needed, PF 5 respirators in most cases provide adequate protection over and above the current label. Current label REIs are 24 hours. For almost every crop/activity combination considered except some low exposure activities, the current REI does not appear to be adequate. Residential handler risks were not considered since thiram is not available for sale to these individuals. Postapplication residential risks are not of concern because only golf course uses have been retained and risks for golfers are not of concern even on the day of application.

Aggregate Assessment

The aggregate exposure assessment was also revised to incorporate the changes made to the dietary and residential exposure assessments. The considerations for aggregate exposure are those from food, water, and residential uses. Since conservative modeling was done to estimate concentrations in drinking water, Drinking Water Levels of Comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper concentration limit for a pesticide in drinking water based on how much of the PAD remains once exposures in food and in the home have been estimated and subtracted.

Aggregate acute and chronic risks resulting from exposure to thiram via dietary (food and drinking water) exposures were assessed (given the current use patterns, no acute or chronic residential exposure scenarios are anticipated). A comparison of the DWLOC and the EECs (Estimated Environmental Concentration) obtained from the PRZM/EXAMS (surface water) and SCIGROW (ground water) models indicate that the drinking water residue contribution to the acute and chronic aggregate risk is not of concern. A short/intermediate term aggregate risk assessment was also conducted. Short-term DWLOCs were calculated based upon average food residues and residential post-application exposure to golfing adults who are exposed to thiram after application to turf. The results indicate that there is no short-term exposure concern for drinking water from groundwater or surface water sources.

DETAILED CONSIDERATIONS

REVIEW OF DEVELOPMENTAL NEUROTOXICITY STUDY

In a developmental neurotoxicity study (MRID 46455201), Thiram technical (99.6% a.i., batch # G410050392) was administered to 24 female Crl:CD® (SD)BR IGS rats/dose in the diet at concentrations of 0, 20, 45 or 90 ppm (0, 1.4, 3.7, and 7.2 mg/kg/day) from

gestation day (GD) 3 through postnatal day (PND) 20¹ at dietary concentrations of 0, 20, 45, and 90 ppm (0, 1.4, 3.7, 7.2 mg/kg/day). The average daily test article intake was 0, 1.4, 3.7, and 7.2 mg/kg/day from GD 3 through GD19 (based on analytical data). A Functional Operational Battery (FOB) was performed on 10 dams/dose on GDs 12 and 18, and on lactation days 4, 11, and 20. On postnatal day 4, litters were culled to yield five males and five females (as closely as possible). Offspring representing at least 20 litters/dose were allocated for detailed clinical observations (FOB), assessment of motor activity, assessment of auditory startle response habituation, assessment of auditory startle pre-pulse inhibition, assessment of learning and memory, and neuropathology at study termination (day 65 of age). On postnatal day 21, the whole brain was collected from 10 pups/sex/dietary level for micropathologic examination and morphometric analysis. Pup sexual maturation was assessed by age at vaginal opening for females and at completion of balano-preputial separation for males.

All dams survived to scheduled termination. Pale skin was observed in eight high-dose dams during the second and third weeks of lactation. Three of these animals showed pale eyes and two had irregular respiration. During in-hand observations of the FOB, 4/12 high-dose females showed pallor on PND 20; three of these animals had cold extremities or were cold to the touch. Also noted at this dose level was an increased incidence of slightly drooping eyes and moderate tremors (4/12 each vs 0 control) on PND 20. In the open field on PND 20, for the control, low-, mid-, and high-dose groups, the mean activity count was 14.8 ± 8.2 , 10.2 ± 4.0 , 12.4 ± 6.3 , and 8.8 ± 6.9 ($p \leq 0.05$), respectively, and the mean rearing count was 7.8 ± 5.7 , 6.0 ± 5.0 , 7.7 ± 5.0 , and 4.4 ± 3.6 , respectively. Clinical signs noted at the high-dose in dams during the exposure period consisted primarily of effects on palpebral closure and tremors. While the control animals exhibited no clinical signs of toxicity on PND 11, 3/12 dams had half-closed or closed eyes and 3/12 experienced slight tremors at the high dose. Similarly, on PND20 6/12 high-dose dams had either drooping, half-closed, or closed eyes and 4/12 had moderate tremors vs 0 incidences of these effects in controls.

Body weight of the high-dose dams was significantly less ($p \leq 0.01$; 94-96% of controls) than that of controls on GDs 6-20 and lactation days 1 and 7-14. Cumulative weight gain by the high-dose group was 8% and 83% (both $p \leq 0.01$) of the control levels during GDs 3-6 and GDs 3-20, respectively. For the mid-dose group, body weight gain was 75% ($p \leq 0.05$) of the control level for GDs 3-6, but was similar to the controls thereafter. During lactation, body weight gain was not affected by treatment in any group. A dose-related decrease in food consumption occurred in all treated groups on GD 3, the first day animals were presented with the treated food. No effects on food consumption were observed in the low- and mid-dose groups during the remainder of gestation. Food consumption by the high-dose group was 69% and 83% (both $p \leq 0.01$) of the control level for GDs 3 and 4, respectively, was $\geq 90\%$ of the control level during GDs 5-16, and was 76-87% of the control level for GDs 17-19. Food consumption was similar between the treated and control groups during lactation. At maternal necropsy, findings in the

¹ Abbreviations: GD = gestation day(s), PND = post-natal day, CV = coefficient of variation

high-dose group included enlarged spleen (6/24), pale liver (3/24) and kidneys (2/24), congested mesenteric lymph nodes (4/24), and dark contents in the lower gastro-intestinal tract (5/24). None of these findings was seen in animals from the control, low-, or mid-dose groups. Mean brain weight was similar between the treated and control groups. **The maternal systemic and neurotoxicity LOAEL for Thiram in rats is 90 ppm in the diet (7.2 mg/kg/day) based on decreased body weight, body weight gain, and food consumption, clinical signs of toxicity, and FOB findings. The maternal NOAEL is 45 ppm (3.7 mg/kg/day).**

No treatment-related effect on the number of litters, live litter size, sex ratio, or live birth, viability, or lactation indices was observed. No dam had total litter loss. No treatment-related clinical signs of toxicity were observed in the offspring during lactation or during the post-weaning period.

During pre-weaning, pup body weight and body weight gain were decreased (\downarrow 6-13% and 14%, respectively) at the high dose. These decreases were sustained during the post-weaning period and were considered toxicologically relevant. In contrast, the decreases in pup body weight and weight gain seen at the mid-dose ($\downarrow \leq 7\%$) were not sustained during the post-weaning period ($\downarrow \leq 4\%$) and were not considered sufficiently robust to be toxicologically relevant. No differences in the mean day to preputial separation for males or vaginal opening for females were observed between the treated and control groups.

No treatment-related effects were found during in-hand observations of offspring on any test day (PND 35, 45, or 60). On PND 4, no differences were seen between pups in the treated and control groups on performance in the open arena. On PND 11, the mean score for surface righting reflex for male pups in the control, low-, mid-, and high-dose groups was 1.0, 1.1, 1.2, and 1.5, respectively, with one high-dose male failing the test. No effects on surface righting reflex were observed in females. On PND 21, rearing count for the control, low-, mid-, and high-dose groups was 3.3, 3.8, 2.9, and 4.8, respectively, for males, and 2.6, 3.3, 3.8, and 4.9, respectively, for females. On PND 21, two females from the high-dose group were observed with occasional chewing movements. Flattened gait was noted for 2, 3, 5, and 4 males in the control, low-, mid-, and high-dose groups, respectively, on PND 60. No treatment-related effects were noted in the open arena on PNDs 35 or 45.

Locomotor activity was increased in males on PND 13 (\uparrow 73%) at 90 ppm dose and in females on PND 17 at dose levels \geq 45 ppm (\uparrow 46-60%). While an increase was also noted in males at the 45 ppm dose level, the toxicological relevance of the effect was considered equivocal due to the high variability (CV = 47%) which was comparable to the magnitude of the change observed (\uparrow 43%). In females, the increase in locomotor activity was seen in conjunction to impaired habituation as evidenced by the observation that locomotor activity was higher during the last sub-sessions than it was during the first sub-sessions. Motor activity was unaffected at other time periods.

On PND 23/24 and 61/62, auditory startle was decreased in males by 15-25% at the highest dose tested. Pre-pulse inhibition was also decreased at this dose level (19.1 ± 8.2

% vs $31.5 \pm 10.8\%$ in control). Auditory startle and pre-pulse inhibition were unaffected in females.

In the Morris water maze, males and females from the high-dose group had longer swimming times and greater number of sector entries during the PND 23/24 and PND 61/62 testing, respectively. No other treatment-related effects on learning and memory were observed in males or females.

During the PND 21 morphometric evaluation, a 7% increase was observed in the hippocampus of males and in the neocortex of females at the highest dose tested. These effects are considered compound-related and toxicologically relevant. Consequently, it is requested that measures for these brain regions at the low-and mid-dose be submitted to the Agency for evaluation.

The offspring systemic and neurotoxicity LOAEL for Thiram in rats is 45 ppm in the diet (3.7 mg/kg/day) based on increased locomotor activity in females on PND17. The offspring NOAEL is 20 ppm (1.4 mg/kg/day).

The DNT study is relevant for both the short- and intermediate term risk assessments. Although a study conducted *via* the most relevant route of exposure (21-day Dermal Toxicity Study in Rabbits) was available for consideration, the DNT was selected since it evaluated endpoints of concern (neurotoxicity) that were not assessed in the Dermal Toxicity Study. If a dermal absorption factor of 1% is applied to the NOAEL obtained in the DNT the derived dermal equivalent dose (DED) would be 150 mg/kg/day. Since the NOAEL from the dermal study is 300 mg/kg/day, use of the DNT would be protective of the effects of concern seen in the dermal toxicity study (decreases in body weight and food consumption; and alterations in clinical chemistry).

The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 1 below.

Table 1. Summary of Toxicological Dose and Endpoints for Thiram			
Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA Safety Factor* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (All Populations)	NOAEL = 5 mg/kg/day UF = 100* Acute RfD = 0.05 mg/kg/day	FQPA SF = 1 aPAD = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ = 0.05 mg/kg/day	Acute Neurotoxicity Study - Rat LOAEL = 150 mg/kg/day based on FOB effects (lethargy, lower temperature, reduced startle response, no tail pinch response), reduced motor activity, and reduced brain weights

Table 1. Summary of Toxicological Dose and Endpoints for Thiram

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA Safety Factor* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13+)	NOAEL = 1.4 mg/kg/day UF = 100* Acute RfD = 0.014 mg/kg/day	FQPA SF = 1 aPAD = <u>acute RfD</u> FQPA SF = 0.014 mg/kg/day	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17
Chronic Dietary (All populations)	NOAEL = 1.5 mg/kg/day UF = 100 Chronic RfD = 0.015 mg/kg/day	FQPA SF = 1 cPAD = <u>chronic RfD</u> FQPA SF = 0.015 mg/kg/day	Combined Chronic Toxicity/Carcinogenicity Study - RAT & Chronic Oral Toxicity Study - DOG LOAEL = 7.3 based on changes in hematology, clinical chemistry, incidences of bile duct hyperplasia, and reduction in mean body weight gain seen at 7.9 mg/kg/day in conjunction with elevated cholesterol levels and increased liver weights reported in the Chronic Oral Toxicity Study in Dogs at 2.6 mg/kg/day
Short-Term Incidental Oral (1-30 days)	NOAEL = 1.4 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17
Intermediate-Term Incidental Oral (1-6 months)	NOAEL = 1.4 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17
Short-Term Dermal (1 to 30 days)	Oral study NOAEL = 1.4 mg/kg/day (Dermal absorption factor = 1%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17
Intermediate-Term Dermal (1 to 6 months)	Oral study NOAEL = 1.4 mg/kg/day (Dermal absorption factor = 1%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17

Table 1. Summary of Toxicological Dose and Endpoints for Thiram

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA Safety Factor* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Long-Term Dermal (>6 months)	Dermal (or oral) study NOAEL= 1.5 mg/kg/day (dermal absorption rate = 1%when appropriate)	Residential LOC for MOE = 1000 Occupational LOC for MOE =100	Combined Chronic Toxicity/Carcinogenicity Study - RAT & Chronic Oral Toxicity Study - DOG LOAEL = 7.3 based on changes in hematology, clinical chemistry , incidences of bile duct hyperplasia, and reduction in mean body weight gain seen at 7.9 mg/kg/day in conjunction with elevated cholesterol levels and increased liver weights reported in the Chronic Oral Toxicity Study in Dogs at 2.6 mg/kg/day
Inhalation (All durations)	Inhalation (or oral) study NOAEL= 1.4 mg/kg/day (inhalation absorption rate = 100%)	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	Dev. Neurotoxicity Study - Rat LOAEL = 3.7 mg/kg/day based on increases in motor activity seen in female offspring on PND 17
Cancer (oral, dermal, inhalation)	NOT LIKELY TO BE CARCINOGENIC TO HUMANS		

*A database uncertainty factor of 10X was applied in addition to the usual inter- and intraspecies safety factor. UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

DIETARY EXPOSURE ASSESSMENT

For acute and chronic assessments, HED is concerned when dietary risk exceeds 100% of the PAD. The DEEM-FCID™ analyses estimate the dietary exposure of the U.S. population and 26 population subgroups. The results reported in Tables 4 and 5 are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years.

Results of Acute Dietary Exposure Analysis

Results are reported at the 99.9th percentile of exposure because the assessment incorporated estimates of %CT. The acute dietary risk for all population subgroups are below 100% of the aPAD (Table 2) and are therefore not of concern.

Table 2. Results of Acute Dietary Exposure Analysis

Population Subgroup	aPAD (mg/kg/day)	95 th Percentile		99 th Percentile		99.9 th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.05	0.000256	<1	0.002567	5.1	0.013970	28
All Infants (< 1 year old)	0.05	0.000053	<1	0.003642	7.2	0.020218	40
Children 1-2 years old	0.05	0.001014	2.0	0.011209	22	0.039088	78
Children 3-5 years old	0.05	0.000925	1.9	0.008303	17	0.036283	73
Children 6-12 years old	0.05	0.000485	<1	0.004467	8.9	0.023055	46
Youth 13-19 years old	0.05	0.000152	<1	0.002035	4.0	0.009914	20
Adults 20-49 years old	0.05	0.000116	<1	0.001822	3.6	0.008696	17
Adults 50+ years old	0.05	0.000264	<1	0.002130	4.2	0.008907	18
Females 13-49 years old	0.014	0.000148	1.1	0.002183	16	0.009563	68

** The values for the highest exposed population for each type of risk assessment are bolded.

Results of Chronic Dietary Exposure Analysis

The results indicate that chronic dietary risk estimates are not of concern for all population subgroups. Exposure estimates for the thiram dietary assessment (including the acute dietary assessment) are considered to be conservative because they are based solely on field trial data.

Table 3. Results of Chronic Dietary Exposure Analysis

Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.015	0.000082	<1
All Infants (< 1 year old)	0.015	0.000092	<1
Children 1-2 years old	0.015	0.000304	2.0
Children 3-5 years old	0.015	0.000249	1.7
Children 6-12 years old	0.015	0.000141	<1
Youth 13-19 years old	0.015	0.000057	<1
Adults 20-49 years old	0.015	0.000050	<1
Adults 50+ years old	0.015	0.000064	<1
Females 13-49 years old	0.015	0.000060	<1

** The values for the highest exposed population for each type of risk assessment are bolded.

OCCUPATIONAL EXPOSURE ASSESSMENT

Occupational Handler Risks

Current thiram labels typically require that handlers wear long pants, long-sleeved shirts, and gloves. Respirators are generally not required. The majority of the scenarios have risks associated with them that meet or exceed the Agency's uncertainty factors for noncancer risk assessments at some level of personal protection (i.e., they are mitigated at some level of personal protection). For most of these, risks were not of concern based on the current label requirements. For approximately one half of the agricultural use (i.e., non-seed treatment) scenarios, risks at the label requirements are of concern and additional levels of personal protection are required to achieve Agency risk targets. In fact, in some cases engineering controls such as closed loading systems are needed. Risks can be reduced to target levels for most scenarios that do not meet risk targets with the use of a protection factor 5 respirator (e.g., a disposable dust/mist type device). Risks for most seed treatment scenarios are not of concern at the level of personal protective clothing/equipment specified by the label. Several data gaps were also identified in the previous assessment and remain unchanged. These include small use areas such as: in-furrow/at-plant applications; repellent paint-on applications; powered backpack; engineering control data for seed treatment; on-farm seed treatment data with different application methods (e.g., admixture); sprinkler can; and bulb dip applications.

Occupational Postapplication Worker Risks

Current label requirements specify 24 hour REIs. For all but the lowest exposure scenarios, risks are not of concern (i.e., MOEs > 100) at the current REI. Most critical cultural activities (e.g., thinning and harvesting) have risks that are of concern at the current REI of 24 hours and, in most cases, risks for these activities do not meet the Agency target uncertainty factor of 100 until approximately 5 to 15 days after application. The uncertainties associated with this assessment should also be considered including strawberry data were used for all assessments, the repellency use pattern is not well defined, and no turf-specific data were available.

Detailed calculations can be found in Appendices A and B.

RESIDENTIAL EXPOSURE ASSESSMENT

Thiram is not available for sale or use by homeowner applicators. In fact, the only retained use that was considered in the assessment was on golf course greens and tees. All thiram turf uses

that would conceivably lead to children's exposure on treated turf have been cancelled by the registrant and as such are no longer included in this assessment. When use is restricted to greens and tees, the duration of exposure is 1 hour to reflect the anticipated time a player would be spending in contact with those areas. Risks are not of concern on the day of application for golfers (i.e., MOEs > 100 on day of application) (Table 4).

Table 4: Summary of Thiram Noncancer Postapplication Residential MOEs For Adults			
Scenario	Descriptor	Results	
		MOE on Day 0	Days MOE _≥ UF
Golfing	16.3 lb ai/A - California Data	1837	0
	24.5 lb ai/A - California Data	1222	3
	16.3 lb ai/A - Florida Data	1837	0
	24.5 lb ai/A - Florida Data	1222	2

Detailed calculations can be found in Appendix C.

AGGREGATE EXPOSURE AND RISK ASSESSMENT

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home. Risk assessments for aggregate exposure consider both short-, intermediate- and long-term (chronic) exposure scenarios considering the toxic effects which would likely be seen for each exposure duration.

Thiram is a food use chemical. Drinking Water Levels of Comparison (DWLOC) have been calculated for thiram. There are residential (non-occupational) uses of thiram; therefore, the considerations for aggregate exposure are those from food, drinking water and residential exposure.

Drinking Water Levels of Comparison (DWLOCs)

A Drinking Water Level of Comparison (DWLOC) is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxic endpoint, with drinking water consumption, and body weights. Different populations will have different DWLOCs.

HED uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. In the absence of monitoring data for pesticides, it is used as a point of comparison against

conservative model estimates of a pesticide's concentration in water. DWLOCs are not regulatory standards for drinking water; however, they do have an indirect regulatory impact through aggregate exposure and risk assessments. DWLOCs for thiram were calculated using the dietary food exposure and default body weight and water consumption figures. For adult males, the default body weight is 70 kg, and water consumption is 2 L; for females, the body weight default is 60 kg with a 2 L water consumption default; and for infants and children, the defaults are set at 10 kg for body weight and 1 L for water consumption.

$$\text{DWLOC}(\mu\text{g/L}) = \frac{[\text{maximum water exposure (mg/kg/day)} \times \text{body weight (kg)}]}{[\text{water consumption (L)} \times 10^{-3} \text{ mg}/\mu\text{g}]}$$

where maximum water exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

Acute Aggregate Exposure and Risk

DWLOCs were calculated for the U.S. population, females 13-49 years old and infants and children. Aggregate acute risks resulting from acute exposure to thiram via dietary (food and drinking water) exposures were assessed. A comparison of the DWLOC and EECs (Estimated Environmental Concentration) obtained from the PRZM-EXAMS (surface water) and SCIGROW (ground water) models indicate that the drinking water residue contribution to the acute aggregate risk are not of concern for any population subgroup.

Table 5. Acute DWLOC Comparison

Population Groups	Dietary Exposure from DEEM analysis	aPAD (mg/kg/day)	Maximum Allowable Drinking Water Exposure (mg/kg/day)	DWLOC _{acute} (μg/L)	PRZM/EXAMS Peak EECs (ppb)	SCIGROW concentration (ppb)
U.S. General Population	0.013970	0.05	0.0360	1260	55	0.84
Females 13- 49	0.009563	0.014	0.0044	132	55	0.84
Infants and Children	0.039088	0.05	0.0109	109	55	0.84

Short/Intermediate Term Aggregate Exposure and Risk

Short-term DWLOCs were calculated based upon average food residues and residential post-application exposure. Surface and ground water concentrations estimated using modeling are below the short-term DWLOC for thiram (Table 6). Consequently, there is no short-term exposure concern for drinking water from groundwater or surface water sources.

Table 6. Short-Term Aggregate Risk and DWLOC Calculations (Inhalation/Dermal Endpoints and NOAELs the Same)

Population	Short -Term Scenario									
	NOAEL mg/kg/day	Target MOE ¹	Max Exposure ² mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure ³ mg/kg/day	Aggregate MOE (food and residential) ⁴	Max Water Exposure ⁵ mg/kg/day	Surface Water EEC ⁶ (ppb)	Ground Water EEC ⁶ (ppb)	Short- Term DWLOC ⁷ (µg/L)
Adult Male	1.4	100	0.014	0.000082	0.0011	1184	0.01280	1.3	0.84	448
Adult Female	1.4	100	0.014	0.000060	0.0011	1206	0.01280	1.3	0.84	384

¹ Short-term dermal and inhalation NOAEL = 1.4 from a developmental neurotoxicity study in rats.

² Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

³ Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]

⁴ Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]

⁵ Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

⁶ The crop producing the highest level was used.

⁷ DWLOC(µg/L) = $\frac{\text{maximum water exposure (mg/kg/day)} \times \text{body weight (kg)}}{\text{[water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$

Chronic Aggregate Risk

Chronic DWLOCs for thiram were calculated using the chronic dietary food exposure and default body weight and water consumption figures. Comparisons between the DWLOCs and the highest EECs of 4.3 ppb(in surface water) and 0.84 ppb (in groundwater) indicate that the level of concern for thiram residues in drinking water has not been exceeded when assessing chronic dietary risk (Table 7). DWLOC calculations were performed for the infant or children subgroup which had the highest exposure.

Table 7. Chronic DWLOCs Comparison

Population Groups	Dietary Exposure from DEEM analysis (mg/kg/day)	cPAD (mg/kg/day)	Maximum Allowable Drinking Water Exposure (mg/kg/day)	DWLOC _{chronic}	PRZM/EXAMS 365 day EECs (ppb)	SCIGROW concentration (ppb)
U.S. General Population	0.000082	0.015	0.0149	522	1.3	0.84
Females (13-49 years)	0.000060	0.015	0.0149	448	1.3	0.84
Children (1-2 years)	0.000304	0.015	0.0147	147	1.3	0.84

Attachments:

Appendix A	Occupational Handler Exposure Spreadsheets
Appendix B	Occupational Postapplication Exposure Spreadsheets
Appendix C	Residential Postapplication Exposure Spreadsheets